FDA AND TOBACCO/NICOTINE ISSUES

Currently, FDA may assert jurisdiction over nicotine- or tobacco-containing food or drug products if those products meet the relevant definitions for "food" or "drug" as provided for in the Federal Food, Drug, and Cosmetic Act (FDC Act). A more complete discussion follows.

Under Sec. 201(g)(1) of the FDC Act [21 U.S.C. 321(g)(1)], "drugs" are defined as: (A) articles recognized in an official compendium, (B) articles intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease, (C) articles (other than food) intended to affect the structure or function of the body, and (D) articles intended for use as a component of a drug. Under Sec. 201(f) of the FDC Act [21 U.S.C. 321(f)], "food" is defined as: (1) articles used for food or drink, (2) chewing gum, and (3) articles used for components of food.

The circumstances in which tobacco- or nicotine-containing products have satisfied these definitions are and have been limited. Historically, FDA has not considered traditional tobacco-containing products, as customarily marketed, to be subject to regulation under the FDC Act. Examples of these types of products are smoking tobacco, cigarettes, cigars, chewing tobacco, and snuff. On December 5, 1977, FDA denied a citizen petition that requested that the Agency assert jurisdiction over traditionally-marketed forms of cigarettes as drugs. This denial was upheld in Action on Smoking and Health v. Harris, 655 F.2d 236 (D.C Cir 1980).

FDA has in the past, however, regulated tobacco products as drugs when health claims were made by the manufacturers or vendors. Two court decisions in the 1950's demonstrate this action on the part of the Agency. In United States v. 46 Cartons, More or Less, Containing Fairfax Cigarettes, 113 F. Supp. 336 (D. N.J., 1953), the court upheld the Agency's action against cigarettes that were being advertised as effective in preventing respiratory and other diseases. In this case the court ruled that such advertising caused these cigarettes to be "drugs" as defined under the FDC Act. In the other case, i.e., United States v. 354 Bulk Cartons Trim Reducing-Aid Cigarettes, 178 F. Supp. 847 (D. N.J., 1959), the court upheld FDA's action against cigarettes that contained tartaric acid - a component that was represented to be effective for combatting obesity. In this case the court ruled that these cigarettes were indeed "drugs" as defined by the FDC Act because of weight-reducing claims made in the advertising and on the cigarette packaging.

2023898731

Source: https://www.industrydocuments.ucsf.edu/docs/rzxj0000

Other examples of regulatory action taken by FDA regarding nicotine-containing products include:

- A Regulatory Letter was issued on February 9, 1987 to the manufacturer (Advanced Tobacco Products) of "Favor Smokeless Cigarettes" and "Favor Smoke-Free Cigarettes", which contained nicotine purportedly derived from tobacco, but no tobacco. These products were represented as novel nicotine-delivery systems and methods of administering nicotine by inhalation of nicotine vapor. In these products, a fibrous plug impregnated with a nicotine solution was inserted into a small plastic tube resembling a conventional cigarette in appearance. The Regulatory Letter advised the firm that "Favor" is a nicotine- delivery system intended to satisfy a nicotine dependence and to affect the structure and one or more functions of the body, and that because of its intended uses, "Favor" is a "drug" as defined under the FDC Act. FDA also advised that, in fact, "Favor" is a "new drug" within the meaning of Sec. 201(p) of the FDC Act because its composition is not generally recognized, among qualified experts, as safe and effective for use under the prescribed or recommended conditions described in its labeling. The manufacturer had disagreed with our conclusion that "Favor" is a "new drug", but suspended distribution and promised to inform the Agency in advance if it contemplated resumption of marketing.

- On April 14, 1989, FDA issued a Regulatory Letter to CA. Blockers, Inc., Louisville, KY, concerning an alcohol-containing cigarette additive marketed under the name "N-Bloctin", and a cigarette product containing such additive marketed under such names as "Optima" and "Spectra". This letter charged that the additive and the cigarette products containing such additive were "new drugs" within the meaning of Sec. 201(p) of the FDC Act, and that they were being marketed without the approval of an NDA in accordance with Sec. 505(a) of the FDC Act. These charges were based on the promotion and labeling for these products that represented them as effective in the prevention of lung cancer and other diseases associated with cigarette smoking by inhibiting the accumulation in the lungs of nitrosamines present in conventional cigarette smoke - claims for which there is no general recognition of safety and effectiveness among qualified experts. In response to this Regulatory Letter the firm advised that it would no longer market these products without prior FDA approval.

2023898732

Source: https://www.industrydocuments.ucsf.edu/docs/rzxj0000

Although regulatory action was not involved, FDA has provided advisory opinions concerning the regulatory status of other tobacco/nicotine-containing products. For example:

- Responding to an inquiry from John Pinney of the Office on Smoking and Health (OSH), on June 23, 1980, FDA Associate Commissioner for Regulatory Affairs, Joseph P. Hile, FDA advised that the product "FREE" satisfied the statutory definition of a "drug" and "new drug" under the FDC Act. Mr. Hile further advised, however, that the Agency did not have the resources to pursue the matter at that time. "FREE" was a non-tobacco smoking product resembling a traditional cigarette in appearance, and was composed of ground cocoa bean shells. The product was labeled and promoted as a nicotine-free smoke, as a means to avoid nicotine's damaging effects on the heart, arteries, respiratory, and digestive systems, and as a means to kick the nicotine habit.

- On September 16, 1987 FDA (CFSAN) advised the developer/manufacturer, The Pinkerton Tobacco Co., Owensboro, KY, that a tobacco-containing chewing gum, marketed briefly by this firm under the name "Masterpiece Tobacs", was a "food" under the FDC Act, and an adulterated food because it contained the ingredient tobacco, which is not generally recognized as safe (GRAS) for use in foods, and there is no regulation authorizing the use of tobacco in chewing gum. The Agency further advised that such product was subject to legal action because it contained a food additive deemed unsafe within the meaning of Sec. 409 of the FDC Act and is, therefore, considered to be adulterated with in the meaning of Sec. 402(a)(2)(C) of the FDC Act.

- In a letter of August 17, 1988 FDA's OTC Compliance Branch provided Polygon International Trading Co., with an opinion on the regulatory status of a non-tobacco "cigarette" made from the leaves of the "Lactuca" plant to be marketed under the brand names "PLENOS", "NONIC", and/or "ALTERN". In that letter the importer was advised that the product was a "drug"/"new drug" under the FDC Act, based on label claims that such product was intended to be used as a smoking deterrent, to eliminate a dependence to nicotine, and to reduce the risk of respiratory, cardiovascular, and other diseases attributed to smoking.

- In a letter of April 18, 1989 from the FDA's OTC Compliance Branch to Jack R. Ormes, Attorney, regarding the proposed importation of "FUTURE FREE" or "FREEDOM",

2023898733

Source: https://www.industrydocuments.ucsf.edu/docs/rzxj0000

a roll-on nicotine product Mr. Ormes was advised that such product was a "drug"/"new drug" under the FDC Act based on label claims that such product would satisfy a nicotine dependence, would be useful as a smoking deterrent, and would reduce a smoker's risk of harmful side effects and diseases such as cancer that have been attributed to tobacco smoking.

- In a letter of April 18, 1989 from the FDA's OTC Compliance Branch to Dominic J. Biondi/Mechtronics Corp., regarding the proposed marketing of "22 TWENTY-TWO SMOKE FREE CIGARETTES", a smokeless "cigarette" product, Mr. Biondi was advised that such product is a "drug"/"new drug" under the FDC Act based on label claims that such product would satisfy a nicotine dependence, would be useful as a smoking deterrent, and would reduce a smoker's risk of the hazards attributed to smoking tobacco.

- By letter dated July 21, 1992 FDA's OTC Compliance Branch advised David I. Rosen/Ultratech Corp., that his proposed "Smokeless Cigarette/Tobacco Square Kit" would be regarded as a "drug"/"new drug" under the FDC Act based on label claims that such product would be useful in smoking cessation for the treatment, prevention, and mitigation of nicotine withdrawal symptoms.

  This proposed kit consisted of a number of small tobacco squares manufactured from standard reconstituted sheet tobacco (cigar wrap), each of which contains 2.75 mg of nicotine, adhesive tape squares to hold these tobacco squares in place, a bottle containing a solution of glycerin and sodium bicarbonate (as a solvent/transfer medium), and a quantity of "smokeless cigarettes", which contain no tobacco and consist of cigarette filter material wrapped in flavored cigarette paper, resembling conventional filtered cigarettes in size, shape, and outward appearance. A tobacco square, saturated with the glycerin/sodium bicarbonate solution, was intended for application to intact skin, using the accompanying adhesive squares, for the transdermal administration of nicotine. The kit's "smokeless cigarette" component was intended for simultaneous use to satisfy the smoker's hand-oral manipulation behavior associated with cigarette smoking.

Thus, although the Agency has not regulated traditional tobacco- or nicotine-containing products, such as cigarettes, FDA has consistently regulated tobacco- and nicotine-containing products, and will continue to do so, when its jurisdiction over such products has been clearly established by law.

2023898734

Source: https://www.industrydocuments.ucsf.edu/docs/rzxj0000

Other FDA activities concerning tobacco/nicotine issues:

- o Although not involving regulatory action or an advisory opinion from FDA, considerable resources were expended in the Agency's review of the regulatory status of the so-called "smokeless cigarette", "PREMIER", and is worth noting -

  In September, 1987, R.J. Reynolds Tobacco Co. announced plans to test market "PREMIER", a "smokeless cigarette" that heated but did not burn tobacco. Peter Hutt and former FDA Commissioner Arthur Hull Hayes discussed this new product with various HHS and FDA officials, including the Assistant Secretary for Health, the Surgeon General, former FDA Commissioner Young, and FDA's General Counsel, Tom Scarlett.

  The product was introduced via test-market in October, 1988, and in July, 1988, top FDA management concluded that it should be regulated as a "drug/new drug". Dr. Young opted to hold "Pathway B" meetings with various consumer, health professional, and trade associations, followed by a public hearing before making an offical Agency decision on the matter. In April, 1988, the Coalition on Smoking OR Health and the AMA petitioned FDA to regulate "PREMIER" as a drug. The product failed to achieve consumer acceptance due to the high-tech nature of the product and the strange odor after lighting it. Test-marketing was halted in February, 1989. FDA responded to COSOH's petition by declaring the matter a moot issue without identifying any final Agency opinion on the regulatory status of such a product under the FDC Act.

In addition, FDA is responsible for evaluating the safety and effectiveness of OTC and Rx drug products that have been or are currently marketed as <u>smoking deterrents</u> or as useful in <u>smoking cessation</u>.

In this regard, a new drug application (NDA) for the nicotine-containing chewing gum marketed as a prescription drug under the name "Nicorette", by Lakeside Pharmaceuticals, Cincinnati, OH, was approved by FDA on January 13, 1984. This product is intended and labeled as an aid to satisfy a nicotine dependency, following cessation of smoking, when combined with a behavior modification program. Before this product was marketed, its safety and effectiveness were evaluated by FDA under the NDA provisions of the FDC Act. The labeling for "Nicorette" that was approved by the Agency under the NDA includes numerous warnings, precaution statements, contraindications, and adverse reaction information for its safe use.

2023898735

Source: https://www.industrydocuments.ucsf.edu/docs/rzxj0000

The known safety concerns involving nicotine accounts for the prescription-only marketing status of "Nicorette".

Most recently, FDA has approved separate NDA's for nicotine transdermal patch delivery systems for prescription use in smoking cessation programs covering treatment periods of up to 3 months:

(1) "Nicoderm" Marion Merrill-Dow/Alza (to be marketed by Lakeside Pharm.) NDA apprvd. 11/7/91

("Nicoderm" is marketed in strengths of 21 mg, 14 mg, and 7 mg.)

(2) "Habitrol" Ciba-Geigy Corp. NDA apprvd. 11/27/91

("Habitrol" is marketed in strengths of 21 mg, 14 mg, and 7 mg.)

(3) "ProStep" Elan Pharm. (Ireland) (to be marketed by Lederle) NDA apprvd. 1/28/92

("ProStep" is marketed in strengths of 22 mg and 11 mg.)

(4) "Nicotrol 16" Cygnus and Kabi Pharmacia (to be marketed by Warner-Lambert) NDA apprvd. 4/22/92

("Nicotrol 16" is a 16-hour sustained release patch unlike the others named above which are all 24-hour sustained-release patches. "Nicotrol 16" is marketed in strengths of 15 mg, 10 mg, and 5 mg.)

With respect to OTC drugs that are or have been marketed over-the-counter as smoking deterrents, FDA is currently evaluating the safety and effectiveness of various ingredients for this use under the Agency's OTC Drug Review. Under this review FDA will establish conditions or monographs (i.e., identifying ingredients and labeling requirements, among other provisions) under which OTC smoking deterrents will be generally recognized as safe and effective. A final monograph for these products is pending.

As of this date, none of the smoking deterrent ingredients that have been deferred to the OTC Drug Review have been shown to be safe and effective for this intended use. However, under agency policy established at the outset of the OTC Drug Review, pending the promulgation of a final monograph and absent evidence of a public health hazard, marketing may continue for OTC ingredients, labeled for use

2023898736

Source: https://www.industrydocuments.ucsf.edu/docs/rzxj0000

as smoking deterrents, that are legitimately deferred to this review, even if the available data has failed to demonstrate safety and effectiveness.

In the Federal Register of 11/7/90 FDA published a final rule affecting eleven (11) of the smoking deterrent ingredients (along with numerous other OTC ingredients for other uses) that had been deferred to the OTC Drug Review for this use. These ingredients represent those for which no substantive comments or safety/efficacy data have been submitted under the review. With respect to these eleven ingredients their continued marketing for this use has been prohibited. This action does not affect, however, some 30 OTC ingredients that have at one time or another been marketed for this use, and are still deferred to the OTC Drug Review pending the publication of a final monograph.

KMBudich:kmb:9/22/92
TOBACO5.KMB

2023898737

Source: https://www.industrydocuments.ucsf.edu/docs/rzxj0000